

What is claimed is:

- Para 1* 1. A method to reduce airway hyperresponsiveness in a mammal, comprising increasing  $\gamma\delta$  T cell action in a mammal that has, or is at risk of developing, a respiratory condition associated with airway hyperresponsiveness.
2. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action comprises increasing the number of  $\gamma\delta$  T cells in the lung tissue of said mammal.
- Para 2* 3. The method of Claim 2, wherein said step of increasing comprises removing  $\gamma\delta$  T cells from said mammal, inducing said  $\gamma\delta$  T cells to proliferate *ex vivo* to increase the number of said  $\gamma\delta$  T cells, and returning said  $\gamma\delta$  T cells to the lung tissue of said mammal.
4. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action comprises activating  $\gamma\delta$  T cells in said mammal.
5. The method of Claim 4, wherein said step of activating  $\gamma\delta$  T cells is performed *ex vivo*.
6. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action comprises administering an agent to said mammal that activates  $\gamma\delta$  T cells in said mammal.
7. The method of Claim 6, wherein said agent is a protein comprising a BiP-binding motif, wherein said protein is administered in an amount effective to induce proliferation of  $\gamma\delta$  T cells in said mammal.
8. The method of Claim 6, wherein said agent is selected from the group consisting of a glycosylated protein and a glycosylated peptide.
9. The method of Claim 6, wherein said agent is selected from the group consisting of polyGT and poly GAT (1:1:1).
10. The method of Claim 6, wherein said agent is selected from the group consisting of: synthetic GC, synthetic AT and other oligonucleotides.
11. The method of Claim 6, wherein said agent is a mycobacterial product.
12. The method of Claim 6, wherein said agent is a *Listeria* cell wall product.
13. The method of Claim 6, wherein said agent is a cardiolipin.

*Sub a3* 14. ~~The method of Claim 6, wherein said agent is tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).~~

15. The method of Claim 6, wherein said agent is an antibody that specifically binds to a  $\gamma\delta$  T cell receptor and activates said  $\gamma\delta$  T cells.

16. The method of Claim 6, wherein said agent is an antibody that specifically binds to a  $\gamma\delta$  T cell receptor (TCR) selected from the group consisting of a murine TCR comprising V $\gamma$ 4 and a human TCR comprising V $\gamma$ 1.

*Sub a4* 17. ~~The method of Claim 6, wherein said agent is targeted to  $\gamma\delta$  T cells in said mammal.~~

18. The method of Claim 17, wherein said agent is targeted to  $\gamma\delta$  T cells in the lung tissue of said mammal.

19. The method of Claim 17, wherein said agent is targeted to  $\gamma\delta$  T cells having a T cell receptor (TCR) selected from the group consisting of a murine TCR comprising V $\gamma$ 4 and a human TCR comprising V $\gamma$ 1.

20. The method of Claim 17, wherein said agent comprises: (a) an antibody that specifically binds to a molecule on the cell surface of  $\gamma\delta$  T cells; and (b) a compound that activates said  $\gamma\delta$  T cells, wherein said compound is linked to said antibody of (a).

21. The method of Claim 18, wherein said compound that activates said  $\gamma\delta$  T cells is selected from the group consisting of: a protein comprising a peptide having a BiP-binding motif, a glycosylated protein or peptide, polyGT, polyGAT (1:1:1), synthetic GC, synthetic AT, a mycobacterial product, a *Listeria* cell wall product, cardiolipin, TNF- $\alpha$ , and an antibody that specifically binds to a  $\gamma\delta$  T cell receptor and activates said receptor.

*Sub a5* 22. ~~The method of Claim 6, wherein said agent is administered to the lung tissue of said mammal.~~

23. The method of Claim 22, wherein said agent is administered by a route selected from the group consisting of inhaled, intratracheal and nasal routes.

- Sub a6* 24. The method of Claim 6, wherein said agent is administered to said animal in an amount effective to reduce airway hyperresponsiveness in said animal as compared to prior to administration of said agent.
25. The method of Claim 6, wherein said agent is administered with a pharmaceutically acceptable excipient.
26. The method of Claim 1, wherein said  $\gamma\delta$  T cell action is increased within between about 1 hour and 6 days of an initial diagnosis of airway hyperresponsiveness in said mammal.
27. The method of Claim 1, wherein said  $\gamma\delta$  T cell action is increased within less than about 72 hours of an initial diagnosis of airway hyperresponsiveness in said mammal.
28. The method of Claim 1, wherein said  $\gamma\delta$  T cell action is increased prior to development of airway hyperresponsiveness in said mammal.
29. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action decreases airway methacholine responsiveness in said mammal.
30. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action reduces airway hyperresponsiveness of said mammal such that the  $FEV_1$  value of said mammal is improved by at least about 5%.
31. The method of Claim 1, wherein said step of increasing  $\gamma\delta$  T cell action improves said mammal's  $PC_{20\text{methacholine}}FEV_1$  value such that the  $PC_{20\text{methacholine}}FEV_1$  value obtained before said step of increasing  $\gamma\delta$  T cell action when the mammal is provoked with a first concentration of methacholine is substantially the same as the  $PC_{20\text{methacholine}}FEV_1$  value obtained after increasing  $\gamma\delta$  T cell action when the mammal is provoked with double the amount of the first concentration of methacholine.
32. The method of Claim 31, wherein said first concentration of methacholine is between about 0.01 mg/ml and about 8 mg/ml.
33. The method of Claim 1, wherein said airway hyperresponsiveness is associated with a disease selected from the group consisting of chronic obstructive disease of the airways and asthma.

34. A method to identify a compound that reduces or prevents airway hyperresponsiveness associated with inflammation, comprising:

- a. contacting a putative regulatory compound with a  $\gamma\delta$  T cell;
- b. detecting whether said putative regulatory compound increases the action of said  $\gamma\delta$  T cell;
- c. administering said putative regulatory compound to a non-human animal in which airway hyperresponsiveness can be induced, and identifying animals in which airway hyperresponsiveness is reduced or prevented as compared to in the absence of said putative regulatory compound;

wherein a putative regulatory compound that increases  $\gamma\delta$  T cell action and that reduces or prevents airway hyperresponsiveness in said non-human animal is indicated to be a compound for reducing or preventing hyperresponsiveness.

35. The method of Claim 34, wherein said step (b) of detecting is selected from the group consisting of measurement proliferation of said  $\gamma\delta$  T cell, measurement of cytokine production by said  $\gamma\delta$  T cell, measurement of calcium mobilization in said  $\gamma\delta$  T cell, measurement of cytokine receptor expression by said  $\gamma\delta$  T cell, measurement of CD69 upregulation by said  $\gamma\delta$  T cell, measurement of upregulation of CD44 by said  $\gamma\delta$  T cell, and measurement of cytoskeletal reorganization by said  $\gamma\delta$  T cell.

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27